REMARKS

Status of the Application

A. Restriction Requirement

On April 5, 2004, the United States Patent and Trademark Office mailed an Office Action which contained a Restriction Requirement in the instant Application. Applicants responded on May 5, 2004, electing provisionally, with traverse, Group I, claims 1-11, 19 and 53, SEQ ID NO:1. In the Office Action mailed June 17, 2004, the Examiner made the Restriction Requirement final.

Applicants hereby request reconsideration of the final action with respect to the Examiner's requirement to elect only one sequence for Examination, as Applicants submit that it is not an undue burden to search SEQ ID NOs: 1-3 (Groups I-III). Applicants point out that there is a high degree of identity amongst these three sequences. SEQ ID NO:1 is the human PDE7A1 sequence. The mouse PDE7A2 sequence, SEQ ID NO:2, has 93.7% identity with SEQ ID NO:1, and the rat PDE7A1 sequence, SEQ ID NO:3, has 94.1% identity with SEQ ID NO:1. Thus, a BLAST search done with SEQ ID NO:1, using, for example, 90% identity as the cut-off, would have revealed SEQ ID NOs:2 and 3. Thus, Applicants submit that it is not unduly burdensome to consider SEQ ID NOs:1-3 in the present application; this number of sequences is a reasonable number of sequences in light of the burden it places upon the Examiner.

Moreover, Applicants respectfully request that the Examiner consider MPEP §803.04, wherein it states that a "reasonable number" of sequences may be claimed in a single application. That section states that up to ten sequences may be considered a "reasonable number" of sequences. Applicants respectfully submit that SEQ ID NOs:1-3 are a reasonable number of sequences, and thus request that these three sequences be fully examined in the present application.

Applicants, therefore, respectfully request that the Examiner reconsider the final action and fully examine SEQ ID NOs: 1-3 in the present Application pursuant to MPEP §803.04.

B. Claims

Claims 1-11, 19 and 53 stand rejected by the Examiner. Claims 12-18, 20-52, and 54-67 have been withdrawn. Claim 3 is being canceled. Claims 1, 2, 4-11, 19 and 53 are being amended. New claims 68-78 are respectfully requested to be entered as indicated herewith.

Claims 1, 2, 4-11, 19 and 53 are being amended to even more clearly point out that which Applicants consider the invention. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Please see, for example, page 64, line 11 through page 67, line 4; page 69, line 9 through page 70, line 26; page 73, line 8 through page 74, line 9; page 76, lines 1-22; page 108, lines 4-18; page 109, lines 5-31; page 110, lines 1-9; page 111, lines 11-14; page 116, lines 15-19; SEQ ID NOs: 1-3; Figs. 2, 6, 7, 12, 13.

Specification

1. The specification is objected to for not complying with sequence rules, because Figure 1 discloses a sequence, but no sequence identifier is shown in Figure 1. Applicants submit that no sequence identifier is included in Figure 1 as the sequences depicted therein are longer than the sequences referred to in any one of SEQ ID NOs:1-3, which are the sequences relevant to the present application.

2. The specification is objected to due to the recitation of "aminoacid", rather than "amino acid". Applicants have made the requested change to the sections of the specification set forth in "Amendments to the Specification" starting on page 3 of this Amendment A. Therefore, Applicants respectfully request that the Examiner reconsider the objections to the specification and withdraw the objection.

Priority

3. The acknowledgement of foreign priority is noted.

Information Disclosure Statement

4. The acknowledgement of the Information Disclosure Statement submitted on January 16, 2002 is noted.

Claim Objections

5. On page 4 of the June 17, 2004 Office Action, the Examiner made claim objections. First, the Examiner states that claims 2-11, 19 and 53 are still partially drawn to non-elected inventions. This is because, the Examiner states, that SEQ ID NO:1 is the elected sequence. However, Applicants submit that, in light of Applicants' above remarks regarding the high degree of identity between SEQ ID NO:1 and SEQ ID NOs:2 and 3, that the burden is not unreasonable, and once again, respectfully request that the Examiner consider SEQ ID NOs:1-3 in the present application. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the objection.

6. On page 4 of the June 17, 2004, Office Action, the Examiner made the claim objection that claims 1, 19 and 53 are objected to because of the recitation of "PDE7" and "L22M2". "PDE7" is being deleted and "phosphodiesterase 7" inserted therefor by the present amendments to claims 1, 19 and 53. "L22M2" is being deleted by the present amendment to claim 1. Applicants respectfully submit that this objection is rendered moot by the present amendments. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the objection.

7. On page 4 of the June 17, 2004, Office Action, the Examiner made the claim objection that claim 3 is objected to due to the recitation of the term "aminoacid". Claim 3 is being canceled without waiver or prejudice, subject to the right to file a divisional application(s) thereto. Thus, the present amendment is rendering moot this objection. Applicants respectfully request that the Examiner reconsider and withdraw the objection.

8. On page 4 of the June 17, 2004, Office Action, claims 19 and 53 are objected to as not being in proper form as required by 37 C.F.R. §1.75. Claims 19 and 53 are being amended. Presently amended claim 19 is now independent. Presently amended claim 53 now depends from claims 1, 2, 4-9 or 68-76.none of claims 1, 2, 4-9 or 68-76 are multiply dependent. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the objection.

9. On page 4 of the June 17, 2004, Office Action, claims 19 and 53 are objected to as they refer to non-elected claims, i.e., claims 12-18. Presently amended claim 19 is now independent. Presently amended claim 53 now depends from claims 1, 2, 4—9 or 68-76. Claims 1, 2, 4-9 and 68-76 are elected claims. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the objection.

10. On page 4 of the June 17, 2004, Office Action, claim 53 is objected to due to the recitation of the term "measures". Consistent with the Examiner's suggestion, "measures" is being deleted and "measurements" inserted therefor. As the Examiner will appreciate the amendments are fully

supported by the specification as originally filed; thus, no new matter is being added by the amendments. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the objection.

Claim Rejections - 35 U.S.C. §101

11-13. Claims 1-11, and 19 stand rejected by under 35 U.S.C. §101 because "the claimed invention is directed to non-statutory subject matter." As noted above, claim 3 is being canceled. Consistent with the Exmainer's suggestion, "isolated or purified" is being inserted into each of claims 1-2, 4-11, and 19. Presently amended claims 1-2, 4-11 and 19 even more particularly point out the non-naturally occurring differences between the claimed products and the naturally-occurring products. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Please see, for example, page 30, lines 11-30, at Example 1 and Example 2 of the specification. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim Rejections - 35 U.S.C. §112, Second Paragraph

14-15. Claims 1-11, 19 and 53 stand rejected under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention."

16. At paragraph 16, pages 5-6 of the June 17, 2004, Office Action, the Examiner states that "Claim 1 "is indefinite in the recitation of 'a polypeptide possessing a ...activity at least about 6 fold, preferably about 8 or 10 fold, most preferably 15 to 20 fold higher than...with the exception of the amino acid sequence disclosed by Michaeli et al...(L22M2)' for the following reasons."

Claim 1 is being amended. More specifically, "a higher phosphodiesterase catalytic activity at least about 6 fold, preferably about 8 or 10 fold, most preferably about 15-20 fold higher than the phosphodiesterase catalytic activity of an endogenous full length PDE7 protein" is being amended to "a higher phosphodiesterase catalytic activity than the phosphodiesterase catalytic activity of an endogenous full length phosphodiesterase7A1 protein or phosphodiesterase7A2 protein." As the Examiner will understand, phosphodiesterase7A1 protein or phosphodiesterase7A2 protein is being used as the basis of the comparison for the higher activity of the claimed mutant. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Please see, for example, page 2, line 10 through page 3 line 4 of the specification. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

17. At paragraph 17, page 6 of the June 17, 2004, Office Action, the Examiner states that claims 3-6 are indefinite in the recitation of "427" since the polypeptide of SEQ ID NO:1 only contains 426 amino acids. Claim 3 is being canceled. Claims 4-6 are being amended. Consistent with the Examiner's suggestion, "427" is being deleted, and "426" is being inserted therefor. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

18. At paragraph 18, page 6 of the June 17, 2004, Office Action, the Examiner states that claims 10-11 are indefinite in the recitation of "at least x% homology or identity." Claims 10 and 11 are being amended. More specifically, "at least x% homology or identity" is being deleted and "at least x% identity" inserted therefor. The amendments are supported in the specification as

originally filed, e.g., at page 34, lines 3-32 through page 35, lines 1-5. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

19. At paragraph 19, page 6 of the June 17, 2004, Office Action, the Examiner states that, for examination purposes, it is assumed that claim 19 reads, "wherein the polypeptide is of human, mouse or rat origin, most preferably human." Claim 19 is being amended. More specifically, "wherein PDE7(A) is of human, mouse, or rat origin, most preferably human" is being deleted and "wherein said endogenous full length phosphodiesterase7 protein is of human mouse or rat origin" inserted therefor. As the Examiner will appreciate the amendments are fully supported by the specification as originally filed; thus, no new matter is being added by the amendments. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim Rejections – 35 U.S.C.§112, first paragraph

20-21. Claims 1-9, 19 and 53 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

The Examiner acknowledges that the specification discloses human, rat and mouse phosphodiesterase 7 prctein sequences. However, the Examiner states "the specification is silent in regard to (1) the structure of other phosphodiesterases (2) other structural homologs of a polypeptide comprising at least 312 amino acids of the polypeptide of SEQ ID NO:1 with the exception of the polypeptides of SEQ ID NO:2 and 3, (3) the structural elements in any phosphodiesterase which would provide the desired degree of enzymatic activity, or (4) the structural elements in any 312 consecutive amino acids of the polypeptide of the SEQ ID NO:1 which can be modified to create a structural

homolog with PDE7 activity." The Examiner also states that, "[w]hile a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, either (1) there is no structural feature which is representative of all the members of the genus of phosphodiesterases recited in the claim or (2) the structural recitation recited, i.e., homolog of a polypeptide comprising at least 312 consecutive amino acids of the polypeptide of SEQ ID NO:1, does not constitute a substantial portion of the genus as the remainder of any polypeptide comprising said structural elements is completely undefined and the specification does not define the remaining strucutal features of members of the genus to be selected. It is noted that no degree of structural homology has been recited."

Applicants respectfully disagree with this rejection. Applicants respectfully direct the Examiner's attention to the description of amino terminal deletion mutants and carboxy terminal deletion mutants set forth in the specification at pages 64-67, wherein the generation of deletion mutants of the PDE7A of the invention is taught. At those pages, primers are set forth which were used by the Applicants to make amino terminal and carboxy terminal deletions using PCR. This work was done by Applicants to map the catalytic domain, and identify a putative inhibitory domain.

As is stated at page 64, lines 15-18, eleven constructs were generated by PCR amplification using the full length PDE7A1 cDNA as template and primers which contained restriction sites (*Bam H1* and *Xba1*) to allow subcloning into *Bam H1/Xba1* site of pcDNA4 (Invitrogen) downstream from the histidine tag. The eleven constructs are illustrated in Figure 2. The structural information provided in the specification by these primers listed at pages 64-67, and the constructs depicted in Figure 2, coupled with the data on functionality provided in Figures 6 and 7 and the description at page 69, line 9 through page 70, line 26; page 73, line 8 through page 74 line 9; page 76, line 1 through page 76, line 22 of the specification, address the first comment by the Examiner which is quoted

above. That is, this structural information, linked with the functional information provided in the specification, (1) gives the structure of other phosphodiesterases (other than SEQ ID NOs:1-3), (2) gives other structural homologs of a polypeptide comprising at least 312 amino acids of the polypeptide of SEQ ID NO:1, and (3) gives the structural elements in any phosphodiesterase which provides the desired degree of enzymatic activity, as is provided in the correlation of structure and function at the citations to the specification provided herein.

Applicants have, in the generation of the amino terminal and carboxy terminal deletion mutants as described at pages 64-67 of the specification and illustrated in Figure 2, for which the sequences of the amino and carboxy terminal ends of each mutant polypeptide are described, determined the structure of a representative number of the members of the claimed genus. Six species of the invention are illustrated in both the mutants described at pages 64-67 and in Figs. 6 and 7. The construction of these deletion mutants, and the assessment of their functionality, as discussed in the specification, illustrate members of the genus of polypeptides which is claimed. Thus, in response to the Examiner's comment, the present application provides the structural elements in a representative number of polypeptides comprising 312 consecutive amino acids of the polypeptide of SEQ ID NO:1 which can be modified to create a structural homolog with PDE7 activity. Each deletion mutant, and the data pertaining to its functionality, is written description support for the claimed genus. Moreover, from this teaching and experimental data in the specification, one of ordinary skill in the art would know that Applicants had possession of the claimed invention at the time the present application was filed.

Applicants, therefore, respectfully request the Examiner to reconsider the Office Action and withdraw the rejection of claims 1-9, 19 and 53 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

22. Claims 1-11, 19 and 53 stand rejected under 35 U.S.C. §112, first paragraph, because "while being enabling for the polypeptide of SEQ ID NO:1, does not reasonably provide enablement for (1) any phosphodiesterase, or (2) any polypeptide comprising a PDE7 catalytic domain which is a structural homolog of a polypeptide comprising at least 312 amino acids of the polypeptide of SEQ ID NO:1." The Examiner further states, "[t]herefore, due to the lack of relevant examples, the amount of information provided, the lack of knolwdge about the critical structural elements required to display the desired function, and the unpredictability of the prior art in regard to function based on identity, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to screen and isolate those polypeptides having any phosphodiesterase activity or PDE7 activity recited in the claims." Applicants respectfully traverse this rejection.

Claim 3 is being canceled.

Presently amended claim 1 (and claims depending therefrom) is limited to polypeptides having at least 90% identity to a human PDE7 amino acid sequence (SEQ ID NO:1). Presently amended claim 19 (and claims depending therefrom) is limited to polypeptides having at least 90% identity to either human, mouse or rat PDE7 amino acid sequences (SEQ ID NOs:1-3).

In addition, the specification teaches the critical structural elements required to provide the desired function. See, for example, pages 64-67 and Figs. 2, 6 and 7. Therefore, it would not require one of ordinary skill in the art to go through the burden of undue experimentation in order to screen and isolate those polypeptides having any PDE7 activity recited in the claims.

Additional support can also be found in the application of the Wands factors.

Applicants have also clearly demonstrated the correlation between structure and function of PDE7A mutants. If one skilled in the art sought to confirm that such a correlation is also valid for any other mutant, all that needs to be done is the generation of the mutant polypeptide, and to confirm the

correlation of activity. This is a low quantity of experimentation, and easily performed.

While no piece of prior art has recognized that the inactivation of the regulatory domain of the phosphodiesterase 7 protein would enhance the polypeptide's catalytic activity, the prior art teaches many methods of generating mutant cDNAs, and thereby, polypeptides, in addition to those exemplified by Applicants' specification.

For at least these reasons, Applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim Rejections – 35 U.S.C. §102

23. Claims 1-11, 19 and 53 stand rejected under 35 U.S.C. §102(b) as being anticipated by Han et al. (J. Biol. Chem 272(26):16152-16157 (1997)). The Examiner states that Han et al. teaches a human alternative splicing variant of PDE7 which is labeled HCP1. A sequence alignment was attached to the Office Action. Applicants respectfully traverse this rejection.

Applicants submit that a prima facie case of anticipation under 35 U.S.C. §102(b) has not been made over claims 1, 2, 4-11, 19 and 53. While a specific sequence is taught in those claims (e.g., either SEQ ID NO:1 or SEQ ID NOs:1-3), Han et al. does not teach any of these sequences. The sequnce disclosed in Han et al. is 456 amino acid in length, whereas SEQ ID NOs:1-3 of the present invention are each 426 amino acids long.

Moreover, Han et al. teaches full length, or nearly full length, regulatory domain. The sequence disclosed in Han et al. is 26 amino acids shorter in length than HCP1 (Michaeli et al.). Further, as the Examiner points out, the sequence disclosed in Han et al., as illustrated in Fig. 1A, is 30 amino acids longer in length than SEQ ID NO:1 at the amino terminus. The presently claimed polypeptides comprise polypeptides with an amino terminus either at amino acid 1 of SEQ ID

NO:1 or an amino terminus further to the carboxy terminus of SEQ ID NO:1. Thus, the claimed polypeptides are at least 30 amino acids shorter at the amino terminus in comparison to the sequence disclosed in Han et al., and, as such, thus are different from the sequence which Han et al. discloses. Thus, the polypeptide of Han et al. does not anticipate presently pending claims.

In addition, Han et al. does not teach the claimed activity. That is, in presently amended claim 1, Applicants teach a higher phosphodiesterase catalytic activity than the phosphodiesterase catalytic activity of an endogenous full length phosphodiesterase7 protein, whereas Han et al. did not disclose either the identification of the regulatory domain of PDE7 or teach an increased activity of phosphodiesterase in the protein identified therein.

For at least these reasons, Han et al. does not anticipate the presently pending claims. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

24. Claims 1-11, 19 and 53 stand rejected under 35 U.S.C. §102(b) as being anticipated by Hoffman et al. (Cell Biochem. Biophys. 28:103-113 (1998)): The Examiner states that Hoffman et al. teaches a rat PDE7 which is 426 amino acids long and is 94.1% identical to the polypeptide of SEQ ID NO:1. The Examiner further states that "claims 1-11, and 19 are directed in part to a human, mouse or rat phosphodiesterase comprising a phosphodiesterase 7 catalytic domain wherein said phophodiesterase is a structural homolog of a polypeptide comprising at least 312 amino acids of SEQ ID NO:1." Applicants respectfully traverse this rejection.

Applicants submit that a prima facie case of anticipation under 35 U.S.C. §102(b) has not been made over claims 1, 2, 4-11, 19 and 53. While a specific sequence is taught in those claims (e.g., either SEQ ID NO:1 or SEQ ID NOs:1-3), Hoffman et al. does not teach any of these sequences. The polypeptide disclosed in Hoffman et al. is 433 amino acids in length, whereas SEQ ID NOs:1-3 are each 426 amino acids in length.

In addition, Hoffman et al. does not teach the claimed activity. That is, in presently amended claim 1, Applicants teach a higher phosphodiesterase catalytic activity than the phosphodiesterase catalytic activity of an endogenous full length phosphodiesterase7 protein, whereas Hoffman et al. did not disclose either the existence of the regulatory domain of PDE7 or teach an activity, let alone a higher activity, of phosphodiesterase in the protein identified therein.

For at least these reasons, Hoffman et al. does not anticipate the presently pending claims. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claim Rejections – 35 U.S.C.§103

25, 27 Claim 53 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Hoffman et al. in view of Han et al. The Examiner states that "claim 53 is directed to a kit to screen for compounds that inhibit PDE7 activity wherein said kit comprises a polypeptide having PDE activity and the reagents required to measure PDE activity." The Examiner further states that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a kit to screen for compounds that inhibit PDE7 activity wherein the kit comprises the polypeptide of Hoffman et al. as well as reagents to measure PDE7 activity." Applicants respectfully traverse this rejection. Applicants submit that a prima facie case of obviousness under 35 U.S.C. § 103(a) has not been presented with respect to claim 53.

Hoffman et al. neither teaches nor provides motivation to make the presently claimed kit of claim 53. As discussed in section (24) above, the sequence disclosed in Hoffman et al. is not the sequence claimed in claims 1, 2, 4-9, 19 or 68-78 (the claims from which claim 53 depends). Therefore, Applicants respectfully disagree with the Examiner's assertion, that it would have been obvious to one of ordinary skill in the art to make a kit to screen for compounds that inhibit PDE7 activity wherein the kit comprises the polypeptide of Hoffman et al. as well as reagents to measure PDE7 activity. Just as described

above for the polypeptide disclosed in Han et al., the Hoffman et al. polypeptide is also not the polypeptide of the kit of presently amended claim 53.

Moreover, neither Hoffman et al. nor Han et al. teach the mutant of the presently claimed invention. In addition, neither Hoffman et al. nor Han et al. disclose the activity of the presently claimed mutant. Furthermore, neither Hoffman et al. nor Han et al. teach or suggest a kit to screen for compounds that inhibit PDE7. Thus, one of ordinary skill in the art would not have been motivated to make the presently claimed kit and would also not have had a reasonable expectation of success.

For at least these reasons, Hoffman et al. in view of Han et al. would not have made the presently claimed invention prima facie obvious to a person of ordinary skill in the art at the time the invention was made. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

26. The subject matter of the presently pending claims was commonly owned the invention covered therein were made,

Conclusion

In view of the above remarks and amendments filed herewith, Applicants believe the Application and all of the pending claims are in condition for allowance and such favorable action is respectfully solicited. The Examiner is respectfully urged to contact the undersigned attorney for purposes of favorable advancing the prosecution of this Application.

Date: 12/17/2004

Respectfully submitted,

Kathleen A. Ranney
Attorney for Applicants
Reg. No. 37,702

Pfizer Inc.
Patent Department, MS 8260-1611
Eastern Point Road
Groton, Connecticut 06340
(860) 715-1139